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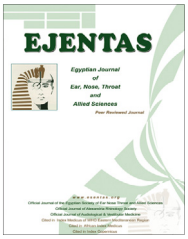

CASE REPORT

Ewing's sarcoma of the maxillary sinus

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Abstract Ewing's sarcoma is typically an aggressive, poorly differentiated tumor affecting children and young adults, it accounts for 4–6% of all primary bone tumors and facial primary localizations occur in only 1–4% of all cases, mostly in the mandible and calvaria. Paranasal sinus involvement is rare. A 22-year-old female was reviewed in Oral & Cranio Maxillofacial Surgery Department. She complained of swelling of the right paranasal area, of one-month duration, progressively increasing in size and associated with pain. The medical history was unremarkable, Contrast Enhanced Computed Tomography scan showed a destructive lesion of the anterior wall of the right maxillary sinus reaching up to the medial wall of the maxillary sinus, other paranasal sinus appearance was normal. Incisional biopsy proved it to be Ewing's Sarcoma. She was treated by chemotherapy using Vincristine, Adriamycin, and Cyclophosphamide alternating with Etoposide & Ifosfamide and Radiotherapy, and this resulted in complete regression of the tumor. Repeated PET scans every 6 months did not suggest any recurrence of the right maxillary sinus tumor. We concluded that treatment by induction chemotherapy followed by radiation therapy leads to a favorable outcome in the above described case, avoiding the morbidity that can result from surgical options.

1. Introduction

Ewing's sarcoma is a malignant, small round cell tumor arising from the bone. First described by James Ewing in 1921 this tumor is of neuroectodermal origin, and it includes many subsets, all of which are referred to as Ewing's family of tumors (EFT).

Ewing's sarcoma (ES) is typically an aggressive, poorly differentiated tumor affecting children and young adults and is rarely seen in older adults.[1] The peak incidence in men is between the ages of 10 and 14 years, whereas in women it is between the ages of 5 and 9 years.[2] White children have an approximately nine fold higher incidence rate of ES than other ethnicities.[1] It accounts for 4–6% of all primary bone tumors[3] and facial primary localizations occur in only 1–4% of all cases, mostly in the mandible and calvaria. Paranasal sinus involvement is rare, and skull base involvement has been infrequently reported.[5]

In the current article we are presenting our experience with a case of maxillary sinus involvement. Clinical presentation,

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radiological evaluation, treatment protocol and results are discussed.

2. Case report

A 22-year-old female was referred to Oral & Cranio Maxillofacial Surgery Department, in January 2011. She complained of swelling of the right cheek first noted one-month ago. This swelling has been progressively increasing in size and associated with pain.

The medical history was unremarkable, and the clinical examination showed a 2×3 cm, firm right para nasal swelling, extending to the infra orbital area. Nasal examination revealed an enlarged inferior turbinate.

Contrast Enhanced Computed Tomography scan (CT) of the face showed a destructive lesion of the anterior wall of the right maxillary sinus reaching up to the medial wall of the maxillary sinus, measures $32 \times 34 \times 33$ mm in its maximal anteroposterior, transverse, craniocaudal dimensions respectively. Other paranasal sinuses appeared normal (Fig. 1).

Thinning out of the orbital floor is noted, with likely extension of the pathological lesion to the right orbit. Subcentimetric bilateral submandibular and deep cervical lymph node enlargements were noted as well.

An incisional biopsy was taken using the Functional Endoscopic Sinus Surgery (FESS technique). The histological findings showed a small round blue cell proliferation. The cells were arranged in sheets and nests with clumped chromatin pattern and scant cytoplasm. Focal cytoplasmic clearing was also observed.

Given the differential of a small round blue cell tumor including neuroendocrine carcinoma, rhabdomyosarcoma, lymphoma etc, a panel of immunoperoxidase stains with appropriates controls was performed. The neoplastic showed strong staining with CD99 and Vimentin, additional stains for epithelial differentiation (Cytokeratin), hematologic and lymphoblastic markers (CD45 and TdT), rhabdoid differentiation (Desmin) and neuroendocrine differentiation (NSE, chromogranin and Synaptophysin) were all negative. These findings are consistent with those of Ewing's sarcoma/PNET.

CT scan of the chest, abdomen and pelvis was done to detect the presence of distant metastasis and the findings were unremarkable, except for mild enlargement of the spleen. Technetium-99 m bone scan did not show any evidence of distant metastatic deposits throughout the skeleton, and bone marrow was free of any neoplastic process.

The case was discussed with the oncologist, and the decision was made to treat the patient by chemo radiotherapy.

The patient was started on systemic intravenous chemotherapy treatment, with VAC alternating with IE protocol. The first cycle of VAC was given on Feb 2011, which consisted of: Vincristine 2 mg, Adriamycin 75 mg/m^2, and Cyclophosphamide 1200 mg/m^2, all given on day one. This was alternated with IE protocol (Etoposide & Ifosfamide).

In June 2011 (after chemotherapy and before radiotherapy), MRI showed a decrease in the size of soft tissue intensity lesion, measuring $17 \times 17 \times 15$ mm in its anteroposterior, transverse, craniocaudal dimensions respectively, denoting disease regression.

Radiotherapy was given for 6 weeks together with IE protocol starting from June 2011, about 3 months after the start of chemotherapy, until August 2011.

In September 2011 (during the chemotherapy) CT scan showed residual small soft tissue density abutting the anterior wall of the right maxillary sinus measuring 10×10 mm with associated mucosal thickening. The chemotherapy was then continued, as before, with alternating protocols VAC and IE until she had completed one year of treatment on February 2012.

Another CT scan after the completion of chemo radiotherapy showed no change in the findings, which may represent underlying fibrosis rather than residual tumor, and this was confirmed with MRI that did not show any significant mass lesion (Fig 2)

Figure 1 Axial CT scan showing involvement of the anterior wall of right maxillary sinus.

Figure 2 Axial CT scan showing fibrosis after chemoradiotherapy.

Repeated PET scans every 6 months, the last February 2014, did not suggest any recurrence of the right maxillary sinus tumor.

3. Discussion

The Ewing's sarcoma family of tumors (EFT) includes ES of bone (ESB), extra osseous ES (EES), peripheral primitive neuroectodermal tumor of bone (pPNET) and malignant small-cell tumor of the thoracopulmonary region (Askin's tumor), all of which are neoplasms of neuroectodermal origin.[1] Ewing's Sarcoma of the facial bones is a rare pathological entity and involvement of the maxilla is even rarer. A rapidly enlarging, often painful mass is the most frequent clinical presentation.[6]

Signs and symptoms may include paresthesia, loss of teeth, and ulceration of the overlying mucosa. Tumor of the maxillary sinus might not be detected until the lesion protrudes into the nasal cavity and oral cavity, which can cause nasal obstruction, epistaxis, and destruction of the palate.[7]

In the case described in the current study, the patient presented with a firm mass on the right para nasal area with no oral or nasal protrusion, and intact oral mucosa.

The CT scan is the radiographic study of choice. The most common radiologic signs in osseous tissue sarcomas are expansion and erosion of the cortical bones, with bone destruction, with or without periosteal thickening. MRI, CT scan, Technetium-99 m scintigraphy, and bone marrow samplings are all diagnostic tools that can be used to detect the presence of distant metastasis, as in this case that showed no metastasis.[2]

According to the National Comprehensive Cancer Network (NCCN) guidelines for bone cancer, definite diagnosis is based on the histopathologic study of a biopsy, and this should be achieved by means of core needle or surgical biopsy.[2] In the current study the incisional biopsy was taken using the Functional Endoscopic Sinus Surgery (FESS technique).

Ewing's sarcoma is one of the small, blue, round cell tumors of childhood. Histologically, the main differential diagnosis includes lymphoma, Rhabdomyosarcoma, Neuroblastoma, Wilms and primitive Neuroectodermal tumor (PNET).

In addition to histochemical analysis, molecular testing can be helpful to identify signature translocations involving the EWS gene (balanced translocation involving chromosomes 11 and 22). These translocations are detectable with both reverse transcriptase polymerase chain reaction (RT-PCR) and fluorescence in situ hybridization (FISH) in formalin-fixed, paraffin-embedded tissue. RT-PCR had a sensitivity of 54% and specificity of 85%. This genetic anomaly can be recognized by the CD99 antibody. Although positive CD99 staining is highly sensitive for PNET/Ewing's sarcoma, however, not specific as many other tumors like lymphoblastic lymphoma may also express CD99.[1]

Diagnosis of PNET/Ewing's sarcoma is made with tumors showing typical morphologic features with supporting immunoprofile and/or molecular findings. The morphologic features include small round cell morphology with round nucleus, scant cytoplasm with fine chromatin with occasional Homer-Wright or Flexner–Wintersteiner rosettes. The immunoprofile includes reactivity with CD99 in the absence of other markers of small round cell tumors with molecular findings of translocations involving the EWS gene. In this case, the tumor cells have small round cell morphology and were strongly positive for CD99. This morphology is in conjunction with the absence of other markers, including synaptophysin. S-100, desmin, Cytokeratin, CD45, MyoD1, and TdT were consistent with a diagnosis of PNET/Ewing's Sarcoma.[1]

Before the development of effective chemotherapy, local control measures alone were used for the treatment of localized ES. A 5-year survival rate of 10–20% subclinical metastatic disease is now assumed to be present in nearly all patients because of the significant relapse rate seen in patients who have undergone local treatment without systemic chemotherapy.[3] The use of adjuvant chemotherapy in EFT began in the early 1970s and has dramatically improved the overall survival[1] with 5-year survival rates up to 70% in many large studies and a 10-year survival of approximately 50%.[3,4,8]

In general, radical surgery is not provided as a primary treatment modality. The current standard treatment of Ewing's sarcoma begins with chemotherapy unless otherwise contraindicated. Even when the tumor appears resectable, patients are submitted to 4–6 cycles of neoadjuvant chemotherapy to eradicate micro metastatic disease and facilitate effective local control measures with wide negative margins.[2]

In the current study the investigations did not show evidence of metastatic disease at the time of presentation, and as the surgical resection would include orbital exenteration to achieve en bloc resection with negative margins, the decision was to start chemotherapy followed by radiation therapy for local control.

It is a significant observation of note that debulking surgery in Ewing's sarcoma does not seem to offer any advantages in terms of local control and its role appears to be limited to palliative aims. Lymph node metastases from Ewing's Sarcoma are very rare. Considering this, it can be argued that elective neck dissection is not indicated.[2]

Recurrence of Ewing's sarcoma of the bone in general is most common within 2 years of initial diagnosis (approximately 80%). The overall prognosis for patients with recurrent Ewing's sarcoma is poor.[9,10]

Ewing's Sarcoma is an aggressive tumor that rarely affects the facial skeleton. Treatment by induction chemotherapy followed by radiation therapy leads to a favorable outcome in the above described case, avoiding the morbidity that can result from surgical options.

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